

CLAIMS

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2 1. An apparatus for parallel operation of a plurality of microreactors comprising:
3 (a) a chamber equipped with at least one element that supports or secures a
4 microreactor tray inside the chamber, wherein the microreactor tray holds a
5 plurality of microreactors; and
6 (b) a supporting component that holds a signal transmission device,
7 wherein the supporting component and microreactor tray are controllably
8 movable with respect to one another.
- 9 2. The apparatus of claim 1, wherein the elements removably support or secure the
10 microreactor tray.
- 11 3. The apparatus of claim 1, wherein the elements engage at least one member that
12 extends from the microreactor tray.
- 13 4. The apparatus of claim 1, wherein the elements are posts that project upward from
14 the floor of the apparatus.
- 15 5. The apparatus of claim 1, wherein the elements are selected from the group
16 consisting of: brackets that project outward from at least one wall of the
17 apparatus, slots or grooves in at least one wall of the apparatus, depressions or
18 cavities in the floor of the apparatus, and reversible fasteners.
- 19 6. The apparatus of claim 1, further comprising:
20 a plurality of support structures that contain or support an actuating
21 device.
- 22 7. The apparatus of claim 6, further comprising a signal transmission device.
- 23 8. The apparatus of claim 6, further comprising a plurality of actuators mounted in
24 the support structures.

- 1 9. The apparatus of claim 6, wherein the support structures are movable with respect
2 to the microreactor tray.
- 3 10. The apparatus of claim 9, further comprising a plurality of rods that constrain
4 movement of the support structures.
- 5 11. The apparatus of claim 9, wherein movement of the supporting component brings
6 the supporting component into contact with a support structure, thereby moving
7 the support structure so as to allow the supporting component to position a
8 sensing device held by the supporting component into operably close proximity to
9 microreactors mounted in or on a microreactor tray installed in the chamber.
- 10 12. The apparatus of claim 11, further comprising at least one spring that extends
11 from the support structure to a wall of the chamber, and wherein movement of the
12 support structure resulting from contact with the supporting component
13 compresses the at least one spring.
- 14 13. The apparatus of claim 12, wherein termination of contact between the support
15 structure and the supporting component releases compression of the at least one
16 spring, thereby resulting in movement of the supporting structure to its previous
17 position.
- 18 14. The apparatus of claim 9, wherein movement of the supporting structures is
19 motorized and synchronized with movement of the supporting component, so that
20 a supporting structure moves to provide space that allows an excitation or sensing
21 device held in the supporting component to be in operably close proximity to
22 reactors mounted in or on the platform.
- 23 15. The apparatus of claim 8, wherein the actuators are electromagnetic actuators.
- 24 16. The apparatus of claim 8, wherein the actuators are solenoids or electromagnets.

- 1 17. The apparatus of claim 1, wherein movement of the supporting component is
2 controllable.
- 3 18. The apparatus of claim 17, wherein movement of the supporting component is
4 controllable in two dimensions.
- 5 19. The apparatus of claim 17, wherein movement of the supporting component is
6 controllable in three dimensions.
- 7 20. The apparatus of claim 1, wherein movement of the supporting component with
8 respect to the microreactor tray brings an excitation or sensing device held in the
9 supporting component into operably close proximity to microreactors mounted in
10 or on the microreactor tray.
- 11 21. The apparatus of claim 1, wherein the supporting component comprises a bracket
12 slidably attached to a rod extending along a wall of the chamber.
- 13 22. The apparatus of claim 1, wherein the supporting component holds a signal
14 transmission device above or below a microreactor tray mounted in the chamber.
- 15 23. The apparatus of claim 1, wherein the supporting component holds a first signal
16 transmission device above a microreactor tray mounted in the chamber and holds
17 a second signal transduction device below the microreactor tray.
- 18 24. The apparatus of claim 1, further comprising a signal transmission device.
- 19 25. The apparatus of claim 24, wherein the signal transmission device conveys a
20 plurality of signals.
- 21 26. The apparatus of claim 24, wherein the signal transmission device comprises an
22 optical fiber.

- 1 27. The apparatus of claim 24, further comprising an excitation source operably
2 coupled to the signal transmission device.
- 3 28. The apparatus of claim 27, wherein the excitation source is located outside the
4 chamber.
- 5 29. The apparatus of claim 27, wherein the excitation source is located in a wall of the
6 chamber.
- 7 30. The apparatus of claim 27, wherein the excitation source comprises an
8 optoelectronic device.
- 9 31. The apparatus of claim 27, wherein the excitation source comprises a light-
10 emitting diode.
- 11 32. The apparatus of claim 27, wherein the excitation source comprises a laser.
- 12 33. The apparatus of claim 27, wherein the apparatus comprises a plurality of
13 excitation sources.
- 14 34. The apparatus of claim 24, further comprising a detector element operably
15 coupled to the signal transmission device.
- 16 35. The apparatus of claim 34, wherein the detector element is located outside the
17 chamber.
- 18 36. The apparatus of claim 34, wherein the detector element is located in a wall of the
19 chamber.
- 20 37. The apparatus of claim 34, wherein the detector element comprises an
21 optoelectronic device.
- 22 38. The apparatus of claim 34, wherein the detector element comprises a
23 photodetector.

- 1 39. The apparatus of claim 34, wherein the detector element comprises a
2 photomultiplier tube.
- 3 40. The apparatus of claim 34, wherein the apparatus comprises a plurality of detector
4 elements.
- 5 41. The apparatus of claim 40, wherein the detector elements comprise photodetectors
6 in a photodetector array.
- 7 42. The apparatus of claim 1, further comprising means for controlling temperature,
8 relative humidity, or both within the chamber.
- 9 43. The apparatus of claim 1, wherein the chamber comprises inlet and outlet ports.
- 10 44. The apparatus of claim 1, further comprising means for controlling gas
11 concentration within the chamber.
- 12 45. The apparatus of claim 1, further comprising an image sensor.
- 13 46. The apparatus of claim 45, wherein the image sensor comprises a photodiode
14 array.
- 15 47. The apparatus of claim 45, wherein the image sensor is contained within a
16 miniature camera.
- 17 48. The apparatus of claim 45, wherein the image sensor is mounted in or on the
18 supporting component.
- 19 49. The apparatus of claim 1, further comprising a microreactor tray that holds at least
20 4 microreactors.
- 21 50. The apparatus of claim 1, wherein the apparatus comprises a lid that seals the
22 interior of the chamber from the external environment.

- 1 51. The apparatus of claim 1, further comprising a plurality of microreactors
2 comprising:
3 a vessel having an interior volume of a milliliter or less; and
4 means for providing oxygen to the vessel at a concentration sufficient to
5 support cell growth.
- 6 52. The apparatus of claim 51, wherein the vessel has an interior volume of 200
7 microliters or less.
- 8 53. The apparatus of claim 51, wherein the vessel has an interior volume of between
9 50 and 200 microliters, inclusive.
- 10 54. The apparatus of claim 51, wherein the vessel has an interior volume of between 5
11 and 50 microliters, inclusive.
- 12 55. The apparatus of claim 51, wherein the means for providing oxygen comprises an
13 aeration membrane, and wherein oxygen diffuses through the membrane into the
14 vessel.
- 15 56. The apparatus of claim 51, further comprising at least one channel extending from
16 and in communication with the vessel.
- 17 57. The apparatus of claim 56, wherein the channel is a microfluidic channel.
- 18 58. The apparatus of claim 51, further comprising a plurality of channels extending
19 from and in communication with the vessel.
- 20 59. The apparatus of claim 51, further comprising means for measuring a parameter
21 of interest within the vessel or a channel in communication with the vessel.
- 22 60. The apparatus of claim 59, wherein the means comprises an optical sensor.

- 1 61. The apparatus of claim 51, further comprising means for measuring at least two
2 parameters of interest within the vessel or a channel in communication with the
3 vessel.
- 4 62. The apparatus of claim 51, wherein the microreactors comprise miniature stirbars.
- 5 63. An apparatus for parallel operation of a plurality of microreactors comprising:
6 (a) a chamber equipped with at least one element that supports or secures a
7 microreactor tray inside the chamber;
8 (b) a supporting component that holds a signal transmission device,
9 wherein the supporting component and microreactor tray are controllably
10 movable with respect to one another; and
11 (c) a plurality of support structures each of which contains or supports an
12 actuating device.
- 13 64. The apparatus of claim 63, wherein the at least one element removably supports
14 or secures a microreactor tray inside the chamber.
- 15 65. The apparatus of claim 63, wherein the support structures are movable with
16 respect to the microreactor tray.
- 17 66. The apparatus of claim 63, further comprising a microreactor tray that holds at
18 least 4 microreactors.
- 19 67. The apparatus of claim 63, further comprising a plurality of microreactors
20 comprising:
21 a vessel having an interior volume of a milliliter or less; and
22 means for providing oxygen to the vessel at a concentration sufficient to
23 support cell growth.
- 24 68. The apparatus of claim 63, further comprising a plurality of actuators.

- 1 69. A microreactor comprising:
2 a first body layer that defines a vessel having an interior volume of less
3 than 1 microliter;
4 a second body layer that defines a headspace located opposite the vessel;
5 and
6 a gas-permeable membrane that separates the vessel interior from the
7 second body layer.
- 8 70. The microreactor of claim 69, further comprising a substrate layer that supports
9 the first body layer;
- 10 71. The microreactor of claim 69, further comprising a third body layer, wherein the
11 third body layer is located between the gas-permeable membrane and the second
12 body layer.
- 13 72. The microreactor of claim 71, wherein the third body layer contacts the gas-
14 permeable membrane.
- 15 73. The microreactor of claim 72, wherein the third body layer serves as a gasket for
16 the gas-permeable membrane.
- 17 74. The microreactor of claim 71, further comprising a substrate layer that supports
18 the first body layer.
- 19 75. The microreactor of claim 69, further comprising a mixer located within the
20 vessel.
- 21 76. The microreactor of claim 75, wherein the mixer comprises a magnetic stirbar.
- 22 77. The microreactor of claim 69, further comprising at least one sensor that detects
23 or measures a parameter of interest within the vessel.

- 1 78. The microreactor of claim 69, further comprising at least one sensor that detects
2 or measures a parameter of interest within the microreactor vessel, headspace, or a
3 channel in communication with either of the foregoing.
- 4 79. The microreactor of claim 78, wherein the sensor is integrated into the first body
5 layer.
- 6 80. The microreactor of claim 77, wherein the microreactor further comprises a
7 substrate layer that supports the first body layer.
- 8 81. The microreactor of claim 69, further comprising at least one sensor that detects
9 measures a parameter of interest within the microreactor vessel, headspace, or a
10 channel in communication with either of the foregoing.
- 11 82. The microreactor of claim 69, further comprising:
12 a sensor that detects or measures dissolved oxygen within the vessel;
13 a sensor that detects or measures pH within the vessel; and
14 a sensor that detects or measures carbon dioxide within the headspace.
- 15 83. The microreactor of claim 69, further comprising a layer that overlies the second
16 body layer.
- 17 84. The microreactor of claim 69, further comprising at least one channel extending
18 from and in communication with the vessel.
- 19 85. The microreactor of claim 84, wherein communication between the channel and
20 the external environment is achieved via one or more valves.
- 21 86. The microreactor of claim 69, further comprising at least one channel extending
22 from and in communication with the headspace.
- 23 87. The microreactor of claim 69, further comprising a pumping system.

- 1 88. The microreactor of claim 87, wherein the pumping system is pressure driven.
- 2 89. The microreactor of claim 87, wherein the pumping system is driven by
3 evaporation.
- 4 90. A method of selecting a strain that produces a desired product or degrades an
5 unwanted compound comprising steps of:
6 culturing a plurality of different strains, each in an individual microreactor
7 mounted in the apparatus of claim 1;
8 measuring the amount of the desired or unwanted product in each of the
9 microreactors; and
10 selecting a strain that produces an optimum amount of a desired product or
11 degrades a maximum amount of the unwanted compound.
- 12 91. A method of performing a fermentation comprising:
13 selecting a cell strain in accordance with the method of claim 90; and
14 culturing the cell strain in a production scale fermentor.
- 15 92. A method of selecting a bioprocess parameter comprising steps of:
16 culturing cells of an organism type in a plurality of individual
17 microreactors mounted in the apparatus of claim 1, wherein the microreactors are
18 operated under conditions in which the value of the bioprocess parameter varies
19 between the individual microreactors and wherein the organism produces a
20 product or degrades a compound;
21 monitoring biomass, product formation, or compound degradation in each
22 of the microreactors; and
23 identifying the value of the bioprocess parameter that results in optimum
24 biomass, optimum product formation, or optimum compound degradation.
- 25 93. The method of claim 92, further comprising the step of:
26 measuring expression of a plurality of genes in the cells.

- 1 94. The method of claim 93, wherein gene expression is measured using a microarray.
- 2 95. The method of claim 92, in which the bioprocess parameter is actively controlled.
- 3 96. A method of performing a fermentation comprising:
4 culturing cells in a production scale fermentor, wherein one or more
5 bioprocess parameters for the production scale fermentor is selected according to
6 the method of claim 92.
- 7 97. A method of selecting a component or reaction parameter for a reaction
8 comprising steps of:
9 dispensing starting components for a reaction to be optimized into a
10 plurality of individual microreactors mounted in the apparatus of claim 1, wherein
11 either at least one starting component or reaction parameter varies between
12 different reactors;
13 allowing the reaction to proceed for a period of time;
14 measuring a reaction output in each of the microreactors; and
15 identifying a reaction component or parameter that results in an optimum
16 value for the reaction output.
- 17 98. The method of claim 97, wherein the reaction output is product formation or
18 substrate removal.
- 19 99. The method of claim 97, wherein the reaction output is measured multiple times
20 during the period of time.
- 21 100. A method of performing a reaction comprising steps of:
22 selecting at least one reaction component or reaction parameter according
23 to the method of claim 97;
24 dispensing reaction components into a production scale reactor; and
25 allowing the reaction to proceed for a period of time.

- 1 101. A method of selecting a reactor comprising steps of:
2 mounting a plurality of individual reactors having different designs or
3 volumes in a microreactor tray that holds a plurality of microreactors;
4 installing the microreactor tray in the apparatus of claim 1;
5 dispensing reaction components into the individual microreactors;
6 allowing the reaction to proceed for a period of time;
7 measuring at least one reaction output; and
8 selecting a microreactor in which the reaction results in an optimum value
9 for the reaction output.
- 10 102. A method of selecting a microreactor comprising steps of:
11 mounting a plurality of individual microreactors having different designs
12 or volumes in a reactor tray that holds a plurality of microreactors;
13 installing the microreactor tray in an apparatus comprising a chamber
14 equipped with a supporting component that holds an excitation or sensing device;
15 dispensing reaction components into the individual reactors;
16 allowing the reaction to proceed for a period of time;
17 measuring at least one reaction output; and
18 selecting a microreactor in which the reaction results in an optimum value
19 for the reaction output.
- 20 103. The method of claim 102, wherein the supporting component is controllably
21 movable.
- 22 104. The method of claim 102, wherein the apparatus further comprises a plurality of
23 support structures each of which contains or supports an actuating device.
- 24 105. A method of monitoring gene expression comprising:
25 culturing cells in a microbioreactor, wherein the microbioreactor
26 comprises a vessel with an interior volume of 200 μ l or less and means for
27 providing oxygen to the interior of the vessel;

1 harvesting some or all of the cells;
2 contacting RNA obtained from the cells, or a nucleic acid transcription
3 product of such nucleic acid, with a microarray comprising probes for a plurality
4 of genes under conditions such that hybridization occurs; and
5 collecting a signal from the microarray, wherein the signal is indicative of
6 the expression level of at least one gene.

7 106. The method of claim 105, wherein the microbioreactor comprises a vessel with an
8 interior volume of 50 μ l or less.

9 107. The method of claim 105, wherein the contacting step employs 500 ng or less of
10 RNA.

11 108. The method of claim 105, wherein 500 ng or less of RNA is used to generate a
12 nucleic acid transcription product.

13 109. The method of claim 105, wherein the nucleic acid transcription product is cDNA.

14 110. The method of claim 105, wherein the nucleic acid transcription product is cRNA.

15 111. The method of claim 105, further comprising the step of:
16 monitoring one or more bioprocess parameters during part or all of the
17 culturing step.

18 112. The method of claim 111, wherein the bioprocess parameter is dissolved oxygen,
19 pH, carbon dioxide, or cell density.

20 113. The method of claim 111, wherein the bioprocess parameter is production of a
21 product or utilization of a substrate.

22 114. The method of claim 111, further comprising the step of:
23 correlating the expression level of at least one gene with a value for one or
24 more bioprocess parameters.

1 115. The method of claim 105, further comprising the step of:
2 selecting a cell strain or culture condition based on the expression level of
3 at least one gene.

4 116. The method of claim 105, further comprising the step of:
5 collecting at least one image of the culture during the culturing step.

6 117. The method of claim 105, further comprising the step of:
7 collecting an optical signal during part or all of the culturing step.
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